GENERAL PATHOLOGY AND PATHOLOGICAL PHYSIOLOGY

Effect of Electrical Stimulation of Right Stellate Ganglion on Cardiac Function in Rats during Postnatal Ontogeny

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In all examined age groups of rats, the threshold amplitude of stellate ganglion stimulation is higher for the positive chronotropic effect than for the inotropic effect. The stimulation produced a more pronounced effect on stroke volume than on heart rate.

Key Words: *right stellate ganglion; stroke volume; heart rate; rat; stimulation; sensitivity; cardiac reactivity*

Sympathetic regulation of the cardiac function was studied using various experimental approaches. The development of this regulation in the postnatal ontogeny [1,2,11,13], during sympathetic deficiency, and under the effect of exogenous catecholamines [3,6,7] was analyzed, the density of adrenoceptors in the heart was determined [14], *etc.* It was found that high heart rate (HR) in ontogeny is associated with high reactivity of the heart to epinephrine and norepinephrine and low reactivity to acetylcholine. The age-related decrease in HR is accompanied by a decrease in heart reactivity to catecholamines and an increase in heart reactivity to acetylcholine [3,7]. The response of stroke volume (SV) to exogenous acetylcholine and catecholamines decreases with age [1,6]. There are data on sensitization of cardiac adrenergic and cholinergic receptors during postnatal ontogeny [2,8]. At the same time, the effect of sympathetic nerves on the cardiac function is little studied because manipulations on sympathetic nerves (especially in small laboratory animals) are difficult.

Here we studied peculiarities of ino- and chronotropic effects on the heart during stimulation of the sympathetic ganglion in rats at various periods of postnatal ontogeny.

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MATERIALS AND METHODS

The study was carried out on random-bred albino rats at the age of 21 days (late suckling period), 42 days (prepubertal period), 56 and 70 days (pubertal period), and 100 day (mature rats). The rats were anesthetized with urethane 25% (1.3 g/kg, intraperitoneal). After fixation of the animal on the operation table, the right stellate ganglion was prepared under an MBS-1 binocular microscope. The ganglion was stimulated for 30 sec via platinum electrodes connected to an ESL-2 electrical stimulator. Under natural conditions, the discharge frequency in postganglionic sympathetic nerve fibers did not surpass 5 Hz [12]. Therefore, heart sensitivity was evaluated by minimum amplitude at a constant stimulation frequency of 4 Hz, which produced 5-15% changes in HR and SV. Reactivity of the heart was determined by the shift and recovery of these parameters in comparison with their initial values. The amplitude of stimulating pulses was chosen individually for each animal. The data were analyzed using a $Conan_m$-2.0c electrophysiological setup. Differential rheogram and electrocardiogram were recorded at rest and after 10-min electrical stimulation.

The data were analyzed by the method of R. M. Baevskii [4], and SV was calculated by the formula [10] with some modifications [5].

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RESULTS

The threshold amplitude (TA) of stimulation producing a SV increasing SV in 21-day-old rats was 0.2 V. The initial SV was 0.0129±0.0020 ml. After stimulation SV increased by 17% (p<0.01, Table 1) and then gradually decreased but did not returned to the initial value over 10 min. Prepubertal and pubertal rats demonstrated the lowest TA: positive changes in SV were observed at stimulation amplitude of 0.09 V and 0.08 V, respectively. These amplitudes were 5-fold lower than in 21-day-old rats, which probably attested to sensitization of cardiac adrenoceptors. In 70- and 100-day-old rats, the TA increased to 0.1 and 0.3 V, respectively. Thus, TA inducing positive shifts in SV was maximum in mature rats, which reflects decreased adrenergic sensitivity of the heart in these animals. The density of adrenergic network in the myocardium increases during postnatal ontogeny. This is paralleled by a decrease in myocardium sensitivity to adrenergic stimuli [9] and weakening of adrenergic influences to the myocardium [1]. After stimulation of the stellate ganglion in 42- and 100-day-old rats SV recovered within 3 min, while in 56-and 70-day-old rats this recovery took 5-7 min (Table 1). In 21-day-old rats SV did not returned to the initial value for 10 min (Table 1). The stimulation-induced changes in HR were similar in all age groups.

TA of stimulating current pulses inducing positive chronotropic effect was 3 V in 21- and 100-day-old rats (Fig. 1), 2 V in 42-day-old rats, and 2.5 V in 56- and 70-day-old rats. Thus, TA producing a positive chronotropic effect on the heart 10-fold surpassed that for SV increase. It is well known that ventricular myocardium of albino rats is characterized by relatively low content of adrenergic plexuses (compared to other laboratory animals) and higher sensitivity to catecholamines [9]. This explains low TA inducing changes in SV. In all age groups except 70-day-old rats, the reaction of SV was negative against the background of stable HR increase, while in 70-day-old rats this reaction was positive (+35%, Fig. 1). These changes in SV persisted for 10 min after stimulation, while HR returned to the initial values after 1-3 min (in 21-, 42-, 56-, and 100-day-old rats) or after 5 min (in 70-day-old rats).

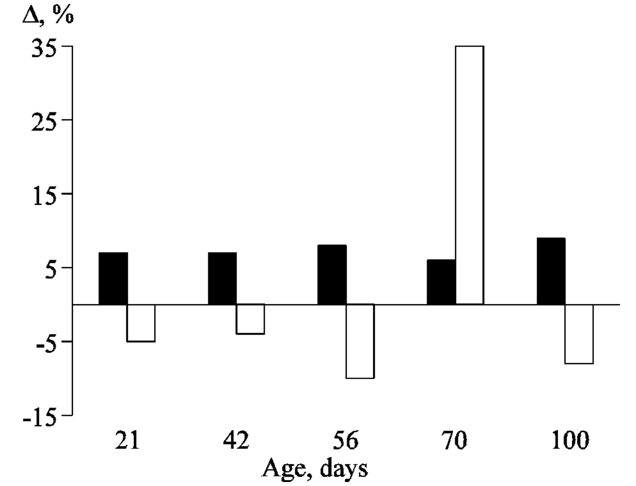

Fig. 1. Changes in HR (solid bars) and SV (light bars) to stimulation of the right stellate ganglion with electrical pulses of a threshold amplitude inducing a positive chronotropic effect.

Threshold stimulation of the right stellate ganglion produced more pronounced changes in SV than in HR. The changes in SV were more pronounced in 21- (17%) and 70-day-old rats (21%). In 42- and 56-day-old rats SV decreased by 12%. The changes in HR induced by treshold stimulation were 6-9% and did not depend on animal age.

Thus, TA of stimulation of the sympathetic ganglion producing changes in SV and HR in 21- and

TABLE 1. Stroke Volume during Stimulation of Right Stellate Ganglion by Threshold Electrical Current in Rats of Different Ages (M±m)

Experimental period	Age, days				
	21 (n=9)	42 (n=11)	56 (n=10)	70 (n=10)	100 (n=7)
Initial level	0.0129±0.0020	0.0204±0.0020	0.0369±0.0040	0.0343±0.0070	0.1327±0.0130
Stimulation	0.0151±0.0020**	0.0229±0.0020**	0.0417±0.0040*	0.0413±0.0080**	0.1518±0.013**
Recovery, min					
1	0.0142±0.0020	0.0217±0.0020	0.0371±0.0040	0.0421±0.0070***	0.1436±0.0140
2	0.0142±0.0020	0.0215±0.0020	0.0377±0.0040	0.0458±0.0090***	0.1403±0.0150
3	0.014±0.002	0.0206±0.0010	0.038±0.005	0.0397±0.0080	0.1368±0.0150
5	0.0137±0.0030	0.0221±0.0020	0.0363±0.0050	0.0375±0.0060	0.1389±0.0110
7	0.0135±0.0020	0.0214±0.0020	0.0356±0.0050	0.0361±0.0070	0.1389±0.0150
10	0.0135±0.0020	0.0212±0.0020	0.0507±0.0120	0.0404±0.0070	0.1434±0.0130

Note. *p<0.001, **p<0.01, ***p<0.05 compared to the initial level (paired Student's test).

100-day-old rats was higher than in other age groups, which indicated low sensitivity of cardiac adrenoceptors to adrenergic stimuli in these rats. In 3-week-old rats (the end of suckling period) cardiotropic adrenerdic influences on the heart become more potent and the content of norepinephrine in the myocardium increases. Accumulation of the neurotransmitter is accompanied by a decrease in the density of α- and β-adrenoceptors [14,15] and cardiac sensitivity to catecholamines in 21- and 100-day-old rats [6]. We observed pronounced changes in the dynamics of parameters of variational pulsogram in 21-day-old rats: the mode amplitude reflecting activity of the sympathetic regulation increased by 19% during stimulation of the stellate ganglion ($p<0.05$), while variational range reflecting activity of the parasympathetic regulation increased by 50% ($p<0.05$). These findings indicate that the 21st day is a critical age for consolidation of the neural cardiotropic regulation in rats.

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REFERENCES

1. R. A. Abzalov and F. G. Sitdikov, *Heart Development under Motor Activity* [in Russian], Kazan' (1998).
2. E. F. Adolph, *Origin of Physiological Regulations*, Moscow (1971).
3. L. A. Aleksandrova and F. G. Sitdikov, in: *Mechanisms of Organism Adaptive Reactions to Physical Loads and Mental Stress* [in Russian], Kazan' (1982), pp. 13-23.
4. R. M. Baevskii, O. I. Kirillov, and S. Z. Kletskin, *Mathematical Analysis of Cardiac Rhythm Variations during Stress* [in Russian], Moscow (1984).
5. R. R. Nigmatullina, F. G. Sitdikov, and R. A. Abzalov, *Fiziol. Zh. SSSR*, **74**, No. 7, 965-969 (1988).
6. F. G. Sitdikov, T. A. Anikina, and R. I. Gil'mutdinova, *Byull. Eksp. Biol. Med.*, **126**, No. 9, 318-320 (1998).
7. F. G. Sitdikov and V. F. Savin, *Fiziol. Zh. SSSR*, **73**, No. 1, 76-82 (1987).
8. V. V. Frol'kis, in: *Physiology of Circulation. Physiology of the Heart*, Ed. E. B. Babskii [in Russian], Leningrad (1980), pp. 350-368.
9. V. N. Shvalev, A. A. Sosunov, and G. Guski, *Morphological Basis of Cardiac Innervation* [in Russian], Moscow (1992).
10. W. G. Kubicek, *Biomed. Eng.*, **9**, 410-416 (1974).
11. M. N. Levy, *Fed. Proc.*, **43**, No. 11, 2598-2602 (1984).
12. C. Polosa, *Can. J. Physiol. Pharmacol.*, **46,** No. 4, 887-896 (1968).
13. S. G. Rockson, C. J. Homsy, P. Quinn, *et al., J. Clin. Invest.*, **67**, 308-312 (1981).
14. W. R. Roeske and K. Wildenthal., *Pharmacol. Ther.*, **14**, 55-66 (1981).
15. A. M. Watanabe, L. R. Jones, A. S. Manalan, and H. R. Jr. Besch, *Circ. Res.*, **50**, 161-174 (1982).